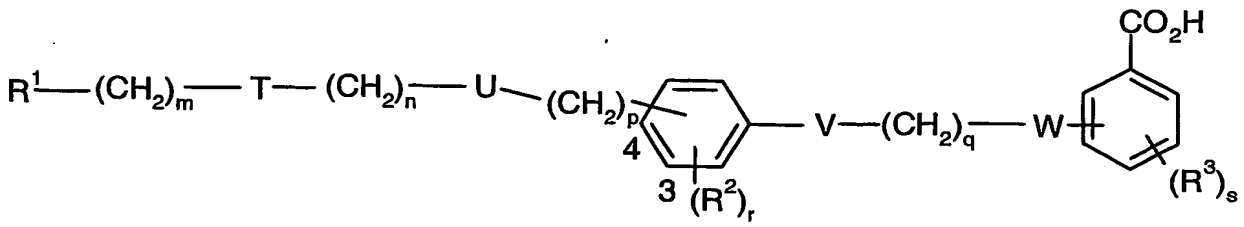
Claims

1. A compound of formula I



I

wherein

R^1 represents aryl optionally substituted by a heterocyclic group or a heterocyclic group optionally substituted by aryl wherein each aryl or heterocyclic group is optionally substituted by one or more of the following groups:

a C_{1-6}alkyl group;

a C_{1-6}acyl group;

arylC_{1-6}alkyl, wherein the alkyl, aryl, or alkylaryl group is optionally substituted by one or more R^b ;

halogen,

-CN and NO_2,

$-NR^cCOOR^a$;

$-NR^cCOR^a$;

$-NR^cR^a$;

$-NR^cSO_2R^d$;

$-NR^cCONR^kR^c$;

$-NR^cCSNR^aR^k$;

$-OR^a$;

$-OSO_2R^d$;

$-SO_2R^d$;

$-SOR^d$;

$-SR^c$;

$-SO_2NR^aR^f$;

$-SO_2OR^a$;

$-CONR^cR^a$;

$-OCONR^fR^a$;

wherein R^a represents H, a C_{1-6}alkyl group, aryl or arylC_{1-6}alkyl group wherein the alkyl, aryl or arylC_{1-6}alkyl group is optionally substituted one or more times by R^b, wherein R^b represents C_{1-6}alkyl, aryl, arylC_{1-6}alkyl, cyano, $-NR^cR^d$, =O, halo, -OH, -SH, $-OC_{1-4}$alkyl, -Oaryl, $-OC_{1-4}$alkylaryl, $-COR^c$, $-SR^d$, $-SOR^d$, or $-SO_2R^d$, wherein R^c represents H, C_{1-4}alkyl, aryl, arylC_{1-4}alkyl and R^d represents C_{1-4}alkyl, aryl, arylC_{1-4}alkyl;

wherein R^f represents hydrogen, C_{1-4}alkyl, C_{1-4}acyl, aryl, arylC_{1-4}alkyl and R^a is as defined above; and

R^k represents hydrogen, C_{1-4}alkyl, aryl, arylC_{1-4}alkyl;

the group $-(CH_2)_m$-T-$(CH_2)_n$-U-$(CH_2)_p$- is attached at either the 3 or 4 position in the phenyl ring as indicated by the numbers in formula I and represents a group selected from one or more of the following: $O(CH_2)_2$, $O(CH_2)_3$, $NC(O)NR^4(CH_2)_2$, $CH_2S(O_2)NR^5(CH_2)_2$, $CH_2N(R^6)C(O)CH_2$, $(CH_2)_2N(R^6)C(O)(CH_2)_2$, $C(O)NR^7CH_2$, $C(O)NR^7(CH_2)_2$, and $CH_2N(R^6)C(O)CH_2O$;

V represents O, S, NR^8, or a single bond;

q represents 1, 2 or 3 ;

W represents O, S, $N(R^9)C(O)$, NR^{10},or a single bond;

R^2 represents halo, a C_{1-4}alkyl group which is optionally substituted by one or more fluoro, a C_{1-4}alkoxy group which is optionally substituted by one or more fluoro, a C_{1-4}acyl group, aryl, an arylC_{1-4}alkyl group, CN or NO_2 ;

r represents 0, 1, 2 or 3 ;

R^3 represents represents halo, a C_{1-4}alkyl group which is optionally substituted by one or more fluoro, a C_{1-4}alkoxy group which is optionally substituted by one or more fluoro, a C_{1-4}acyl group, aryl, an arylC_{1-4}alkyl group, or CN ;

s represents 0, 1, 2 or 3 ; and

R^4, R^5, R^6 , R^7, R^8 , R^9 and R^{10} independently represent H, a C_{1-10}alkyl group, aryl or an arylC_{1-4}alkyl group or when m is 0 and T represents a group $N(R^6)C(O)$ or a group $(R^5)NS(O_2)$ then R^1 and R^6 or $R^1$and R^5 together with the nitrogen atom to which they are attached represent a heteroaryl group;

and pharmaceutically acceptable salts thereof ;

with the provisos that when

1) when R^1 is phenyl optionally substituted by one or two groups independently selected from halo, a C_{1-4}alkyl group which is optionally substituted by one or more fluoro, a C_{1-4}alkoxy group which is optionally substituted by one or more fluoro;

m is 1;

T is $N(R^6)C(O)$ wherein R^6 represents a C_{2-8}alkyl group which is optionally interrupted by oxygen;

n is 1;

U is absent or represents methylene;

p is 0;

r is 0;

V is O or S;

q is 1; and

W is a single bond attached to the position ortho to the carboxylic acid group;

then s does not represent 0; and

2) when R^1 is phenyl optionally substituted by one or two groups independently selected from halo, a C_{1-4}alkyl group which is optionally substituted by one or more fluoro, a C_{1-4}alkoxy group which is optionally substituted by one or more fluoro;

m is 1;

T is $N(R^6)C(O)$ wherein R^6 represents an unbranched C_{2-7}alkyl group;

n is 1;

U is O;

p is 0;

r is 0 or 1;

and when r is 1 R^2 is attached at the 3 position and is OCH_3;

V is a single bond;

q is 2; and

W is O or S attached to the position ortho to the carboxylic acid group;

then s does not represent 0.

2. A compound according to claim 1 in which R^1 represents phenyl which is optionally substituted by one or more of the following: halo, hydroxy, a C_{1-4}alkyl group which is optionally substituted by one or more fluoro, a C_{1-4}alkoxy group which is optionally substituted by one or more fluoro, benzyloxy, a C_{1-4}alkylsulphonyloxy group, phenyl or a heteroaryl group, or R^1 represents heteroaryl which is optionally substituted by one or more of the following: halo, a C_{1-4}alkyl group which is optionally substituted by one or more fluoro, a C_{1-4}alkoxy group which is optionally substituted by one or more fluoro or phenyl optionally substituted by one or more of the following: halo, a C_{1-4}alkyl group which is optionally substituted by one or more fluoro, a C_{1-4}alkoxy group which is optionally substituted by one or more fluoro.

3. A compound according to any previous claim in which the group $-(CH_2)_m-T-(CH_2)_n-U-(CH_2)_p-$ is attached at the 4 position in the phenyl ring as indicated by the numbers in formula I , that is para to the group V.

4. A compound according to any previous claim in which the group $-V-(CH_2)_q-W-$ represents a group selected from : OCH_2, SCH_2, $NHCH_2$, CH_2CH_2S or CH_2CH_2O.

5. A compound according to any previous claim in which the group $-V-(CH_2)_q-W-$ represents the group OCH_2.

6. A compound according to any previous claim in which the group -V-$(CH_2)_q$-W- is joined at the ortho position with respect to the carboxylic acid group.

7. A compound according to any previous claim in which R^2 is halo, a C_{1-4}alkyl group or a C_{1-4}alkoxy group and r is 0 or 1.

8. A compound according to any previous claim in which s is 0.

9. A compound selected from one or more of the following:

3-{[(3-{[(1,1'-biphenyl-4-ylcarbonyl)amino]methyl}phenyl)amino]methyl}benzoic acid;

2-{[4-(2-oxo-2-{[4-(trifluoromethyl)benzyl]amino}ethyl)phenoxy]methyl}benzoic acid;

2-[(3-{2-[benzyl(hexyl)amino]-2-oxoethyl}phenoxy)methyl]benzoic acid;

2-{[3-(2-oxo-2-{[4-(trifluoromethyl)benzyl]amino}ethyl)phenoxy]methyl}benzoic acid;

2-[(4-{3-[[2-(3,4-dimethoxyphenyl)ethyl](methyl)amino]-3-oxopropyl}phenoxy)-methyl]benzoic acid;

2-[(4-{2-[({4-methyl-2-[4-(trifluoromethyl)phenyl]-1,3-thiazol-5-yl}carbonyl)amino]-ethyl}phenoxy)methyl]benzoic acid;

2-({4-[2-({[(2,4-difluorophenyl)amino]carbonyl}amino)ethyl]phenoxy}methyl)benzoic acid;

2-[(4-{2-[(2-methyl-5-phenyl-3-furoyl)amino]ethyl}phenoxy)methyl]benzoic acid;

2-[(4-{2-[(benzylsulfonyl)amino]ethyl}phenoxy)methyl]benzoic acid;

2-[(4-{2-[benzyl(hexyl)amino]-2-oxoethyl}-2-fluorophenoxy)methyl]benzoic acid;

2-[(4-{2-[benzyl(hexyl)amino]-2-oxoethyl}-2-methoxyphenoxy)methyl]benzoic acid;

2-({4-[3-(3,4-dihydroisoquinolin-2(1*H*)-yl)-3-oxopropyl]phenoxy}methyl)benzoic acid;

2-[(4-{2-[4-(1*H*-imidazol-1-yl)phenoxy]ethyl}-phenoxymethyl]benzoic acid;

2-{[4-(2-{4-[(methylsulfonyl)oxy]phenoxy}ethyl)phenoxy]methyl}benzoic acid;

2-[(3-{2-[4-(benzyloxy)phenoxy]ethyl}phenoxy)methyl]benzoic acid;

2-{[3-(2-{4-[(methylsulfonyl)oxy]phenoxy}ethyl)phenoxy]methyl}benzoic acid;

2-({3-[2-(4-hydroxyphenoxy)ethyl]phenoxy}methyl)benzoic acid;

2-[(4-{3-[4-(benzyloxy)phenoxy]propyl}phenoxy)methyl]benzoic acid;

2-{[4-(3-{4-[(methylsulfonyl)oxy]phenoxy}propyl)phenoxy]methyl}benzoic acid;

2-({4-[3-(4-hydroxyphenoxy)propyl]phenoxy}methyl)benzoic acid;

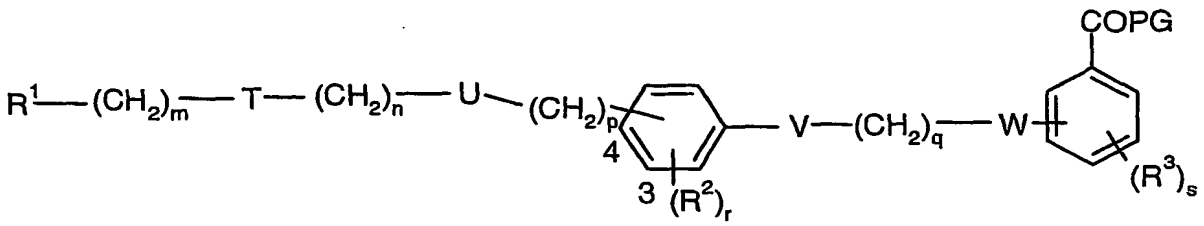
2-{[4-(3-{[2-(2-ethoxyphenyl)ethyl]amino}-3-oxopropyl)phenoxy]methyl}benzoic acid;
2-[(4-{3-[ethyl(2-pyridin-2-ylethyl)amino]-3-oxopropyl}phenoxy)methyl]benzoic acid;
2-{[2-(3-{2-[benzyl(hexyl)amino]-2-oxoethoxy}phenyl)ethyl]thio}benzoic acid;
2-{[4-(2-{heptyl[2-(2-methoxyphenyl)ethyl]amino}-2-oxoethyl)phenoxy]methyl}benzoic acid;
2-[(4-{2-[[2-(4-chlorophenyl)ethyl](heptyl)amino]-2-oxoethyl}phenoxy)methyl]benzoic acid;
2-[(4-{2-[heptyl(2-phenylethyl)amino]-2-oxoethyl}-phenoxy)methyl]benzoic acid;
2-[(4-{2-[ethyl(2-fluorobenzyl)amino]-2-oxoethoxy}phenoxy)methyl]benzoic acid;
2-[(4-{2-[ethyl(2-fluorobenzyl)amino]-2-oxoethyl}benzyl)oxy]benzoic acid;
2-[(4-{2-[heptyl(2-phenylethyl)amino]-2-oxoethyl}benzyl)oxy]benzoic acid;
2-{2-[4-(2-{isobutyl[4-(trifluoromethyl)benzyl]amino}-2-oxoethoxy)phenyl]ethoxy}-benzoic acid; and
2-[(4-{2-[[2-(4-chlorophenyl)ethyl](heptyl)amino]-2-oxoethyl}benzyl)oxy]benzoic acid and pharmaceutically acceptable salts thereof.

10. A pharmaceutical formulation comprising a compound according to any preceding claim in admixture with pharmaceutically acceptable adjuvants, diluents and/or carriers.

11. A method of treating or preventing insulin resistance comprising the administration of a compound according to any one of claims 1 to 9 to a mammal in need thereof.

12. The use of a compound according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of insulin resistance.

13. A process to prepare compounds of formula I comprising reacting a compound of formula II



II

in which R^1, T, U, V, W, R^2, R^3, m, n, p, q, r and s are as previously defined and PG represents a protecting group for a carboxylic hydroxy group with a de-protecting agent.

14. Compounds of formula II as described in claim 13.